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## PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)

VPI/03-101 US

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Typed or printed name \_\_\_\_\_

Application Number

10/798,766

Filed

March 11, 2004

First Named Inventor

Francois Maltais

Art Unit

1624

Examiner

Kosack, Joseph R.

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

I am the

☐ applicant/inventor.

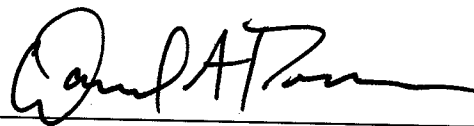
☐ assignee of record of the entire interest.  
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.  
(Form PTO/SB/96)

☒ attorney or agent of record.

Registration number 58,053

☐ attorney or agent acting under 37 CFR 1.34.

Registration number if acting under 37 CFR 1.34 \_\_\_\_\_



Signature

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Typed or printed name

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Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below\*.

☐ \*Total of \_\_\_\_\_ forms are submitted.

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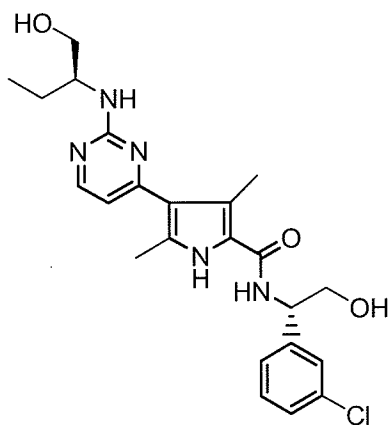
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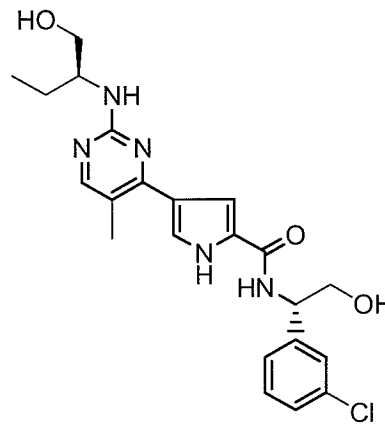
### **PRE-APPEAL BRIEF REQUEST FOR REVIEW**

#### *The rejection under 35 U.S.C. § 103(a)*

In the January 14, 2008 Final Office Action dated January 14, 2008 (hereafter, "the final office action"), the Examiner rejected claims 1, 7, 9-12, and 14 under 35 U.S.C. § 103(a) as allegedly being obvious over Cao et al., International Patent Publication No. WO 2002/64586 (hereafter, "Cao") in view of *In re Wood*, 199 USPQ 137 (hereafter, "Wood"). In particular, the Examiner first limited the examined subject matter to that of the elected species (compound I-51, see below) and then found the instant claims *prima facie* obvious over Example 232 of Cao (see below).



I-51



Example 232 of Cao

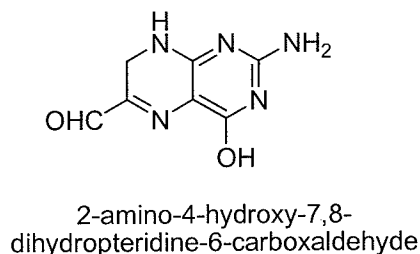
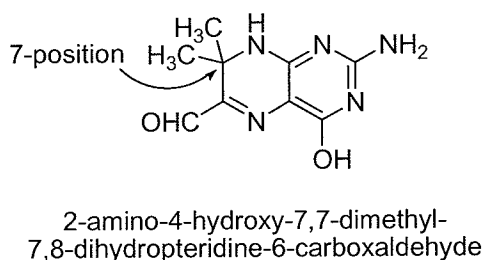
Specifically, the Examiner stated that hydrogen and methyl are deemed obvious variants in view of Wood (page 6, paragraph 3 of the final office action). Accordingly, the Examiner alleged that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to follow the synthetic scheme of Cao and substitute methyl for hydrogen where needed in the pyrimidine and pyrrole rings of Example 232 of Cao to make and use the claimed invention with a reasonable expectation of success. See paragraph 4 on page 6 of the final office action. This obviousness rejection is improper

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because the Examiner has misapplied the holding of Wood and has failed to identify a reason that would have prompted a person of ordinary skill in the art to make the claimed invention.

The argument presented by the Examiner is not sufficient for establishing the *prima facie* obviousness of compound I-51 over Cao. First, the synthetic scheme of Cao was not followed in the preparation of compound I-51. Compound I-51 was prepared via the reaction of Bredereck's reagent and 4-acetyl-3,5-dimethyl-1*H*-pyrrole-2-carboxylic acid, ethyl ester (see Scheme II of page 40 and Examples 1-4 and 7 on pages 56-58 of the present application) and Example 232 of Cao was prepared by an alternative route (see Scheme I on page 77 of Cao). Thus, contrary to the Examiner's assertion, the synthetic procedures of Cao would not have motivated a person skilled in the art to make compound I-51.

The Examiner's *prima facie* obviousness allegation also mischaracterizes Wood, which does not state that hydrogen and methyl are obvious variants. Instead, Wood held that 2-amino-4-hydroxy-7,7-dimethyl-7,8-dihydropteridine-6-carboxaldehyde was obvious in view of the disclosure of 2-amino-4-hydroxy-7,8-dihydropteridine-6-carboxaldehyde because of the close structural similarity between these two compounds. See below for the structures of these compounds. The claimed invention in Wood was found obvious over the prior art because methyl groups were substituted for hydrogens at a single position, the 7-position of the molecule.



In contrast, as has been pointed out in the Reply to August 16, 2007 Office Action that was filed on November 15, 2007 (hereafter, "the November Reply"), there are 32 possible substitution patterns for pyrimidine-pyrrole rings analogous to compound I-51,

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where a hydrogen or methyl group can occupy one or more of the five substitutable positions. See page 19 of the November Reply. Cao exemplifies 238 compounds, including Example 232. None of these compounds has a pyrimidine-pyrrole substitution pattern similar to that of compound I-51. Further, unlike Wood, where there was a substitution at a single position, compound I-51 differs from Example 232 of Cao at three different positions of the molecule. Accordingly, Wood does not support the Examiner's *prima facie* obviousness rejection over Cao.

Furthermore, in order to find a *prima facie* case of obviousness, "a showing that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention [is] also required. ... [I]n cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound" (emphasis added). See *Takeda v. Alphapharm* (Fed. Cir. 2007; 492 F.3d 1350), citing *In re Jones* (Fed. Cir. 1992); *In re Dillon* (Fed. Cir. 1990), *In re Grabiak* (Fed. Cir. 1985), and *In re Lalu* (Fed. Cir. 1984). Nothing in Cao provides the reason to modify Example 232 of Cao in the particular manner required to transform it into compound I-51. A person skilled in the art would have no reasonable expectation of success due to the three distinct changes made in compound I-51 compared to Example 232 of Cao. Accordingly, the obviousness rejection of claims 1, 7, 9-12, and 14 should be withdrawn.

### *Conclusion*

As stated herein, compound I-51 is not taught or suggested by Cao, nor has any rationale been identified that would have led a chemist to modify the synthetic procedures of Cao in the particular manner used to make the compounds of the present invention. In addition, because of the multiple structural differences between the compounds of Cao and those of the present invention, there is no reasonable expectation that the compounds of the present invention would be useful for the inhibition of ERK2 kinase. Therefore, applicants

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respectfully request that the obviousness rejection of the Final Office Action be withdrawn and the scope of the examined subject matter be expanded to include that of amended claims 1, 7-12, and 14.

Respectfully submitted,



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